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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,881	06/29/2005	Robin Mark Bannister	GJE-7147	1605

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EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,881	BANNISTER ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *13 December 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the 371 of PCT/GB03/02586 filed December 13, 2004. Amended claims 1-10 are being examined on the merits herein.

Specification

The disclosure is objected to because of the following informalities: the word preferred is misspelled "preferrred" (page 2, line 23); the drug name dexamethasone is misspelled "dexamethasome" (page 3, line 23). Appropriate correction is required.

Claim Objections

Claim 10 is objected to because of the following informalities: the drug name dexamethasone is misspelled "dexamethasome". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation that "analogs" of

histamine are used in the instantly claimed compositions and methods renders the claims indefinite. "Analog" is a term used in the art to refer to compounds that are similar in structure and activity to a reference compound. However, there is no standard in the art for determining what degree of structural similarity a compound must possess to be an analog. Further, the process of developing analogs that retain the activity of the parent compound is highly unpredictable. It is as of yet impossible to predict what structural modifications can be made to a compound to produce an "analog" that retains the desired activity. The term "analog" is also not defined in the specification as referring to any specific compounds. Thus, it is not clear what compounds are considered "analogs" of histamine and comprise the instantly claimed compositions. Thus, the metes and bounds of patent protection sought for the instantly claimed compositions and methods have not been defined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Mimoz et al and McLintock et al.

The instant claims recite administering nefopam to patients in need of treatment of nausea or emesis (claim 1), wherein the condition is post-operative (claim 2), associated with pain (claim 3), induced by surgery (claim 4), drug-induced (claim 5), and induced by an opioid analgesic (claim 7).

Mimoz discloses a post-operative study on the effects of analgesia with morphine alone (an opioid analgesic), or in combination with nefopam (abstract).

Mimoz teaches that patients underwent abdominal surgery and were monitored on their recovery based on several factors, one of which was nausea. The patients were administered morphine for the pain (page 520, column line 1-5). The reference further teaches that administration of morphine may be associated with various side-effects, including nausea (page 523, column 1, lines 14-16).

Additionally, Mimoz teaches that patients on the combination therapy had a greater sense of analgesia and a reduced sense of nausea as compared to morphine alone (page 524, column 2, lines 1-19).

Mimoz teaches that nefopam, when given in combination with morphine, acts as an anti-emetic and demonstrates a significant morphine-sparing effect (page 524, column 2, lines 10-13).

Similarly, McLintock discloses a post-operative upper abdominal study whereby patients were given morphine with nefopam and morphine with a placebo in order to assess the morphine-sparing effects of nefopam. McLintock teaches that in addition to significant analgesic effects (abstract), the frequency

of side-effects (ie, nausea and vomiting) is reduced when nefopam is given in comparision to placebo (page 780, table 4).

Thus McLintock also teaches that when nefopam is given in combination with morphine, it acts as an anti-emetic agent.

Thus Mimoz and McLintock anticipate the instantly claim invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mimoz et al. in view of Sridhar.

As per claim 1, 5, and 6, Mimoz teaches that nefopam, when given in combination with morphine, demonstrates a significant morphine-sparing effect and acts as an anti-emetic (page 524, column 2, lines 10-13).

Mimoz does not teach the use of nefopam as an anti-emetic agent induced by chemotherapy.

Although it is common knowledge that one of the common side effects of chemotherapy is emesis, Sridhar teaches that this debilitating side effect is the

major cause of cessation of effective cancer chemotherapy in some patients. Furthermore, Sridhar teached that nausea and vomiting can be potentially fatal toxicities in those patients with curable diseases who refuse therapy (page 1508, column I, lines 12-16).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have, in addition to treating nausea induced by conditions such as radiation, toxins, pregnancy, alcohol withdrawal, nicotine withdrawal, drug withdrawal, vestibular disorder, motion, post-operative sickness, surgery, gastrointestinal obstruction, reduced gastrointestinal mobility, visceral pain or increased or decreased intracranial pressure, as recited in claim 4, to have also treated nausea arising from chemotherapy, as taught in Sridhar, with nefopam acting as an anti-emetic agent, as taught in Mimoz. The motivation would have been to attenuate the commonly known side effects of chemotherapy (ie.,nausea and vomiting), increase the quality of life, and decrease the risk of patient non-compliance.

Claims 1 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mimoz et al. in view of Sridhar et al.

Claim 8 recites that in addition to nefopam, the patient is also administered another agent that has anti-emetic properties, wherein said agent can be from the group consisting of phenothiazines, $5HT_3$ receptor antagonists, dopamine antagonists, anticholinergic agents, anti-histamines, histamine analogues, cannabinoids, corticosteroids, GABA receptor antagonists, NK1

receptor antagonists, and α2 and α3 adrenoceptor antagonists (claim 9), namely an agent selected from the group consisting of cyclizine, dolasetron, granisetron, andansetron, tropisetron, nabilone, scopolenine, cinnerizine, promethazine, betahistine, dexamethasone, methylpredrisolone, metoclopramide, chlorpromazine, perphenazine, prochlorperazine, thiethylperazine, droperidol, domperidone and haloperidol (claim 10).

Mimoz is discussed above. Mimoz does not teach the administration of a second agent with anti-emetic properties from the classes of agents as recited in claim 9 and the specific agents in claim 10.

Sridhar teaches that nausea and vomiting occur in a majority of patients receiving cisplatin chemotherapy despite prophylactic single agent anti-emetic therapy. The reference teaches that the combination of three potent anti-emetics, metoclopramide, diphenhydramine, droperidol, and dexamethasone was highly efficacious in preventing nausea and vomiting in moderate or high-dose cisplatin chemotherapy with little toxicity (abstract).

Sridhar further teaches that it may be essential to combine anti-emetics which differ in their ability to block the emetogenecity of chemotherapeutic agents at various trigger zones to produce a synergistic or additive effect (pg 1513, column II, lines 5-9).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have used nefopam as an agent with anti-emetic properties as taught in Mimoz in combination with one or multiple anti-emetic

agents as a combination therapy as taught in Sridhar as a method of treating emesis.

Generally, if it is known to use A, and known to use B for the same purpose, then it is obvious to use both A and B, *In re Susi,* 169 USPQ 423, 426; *In re Kerkhoven,* 205 USPQ 1069.

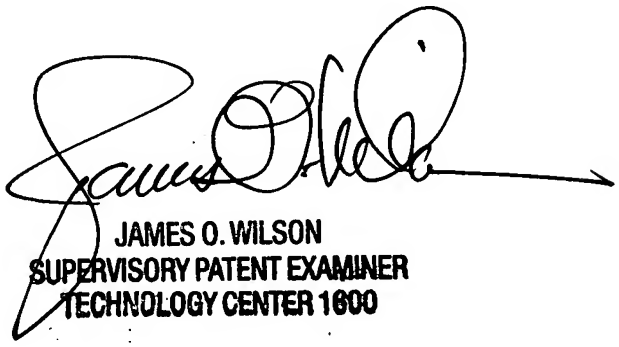
Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY STUCKER can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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